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# Subtotal parathyroidectomy *versus* total parathyroidectomy with autotransplant in secondary hyperparathyroidism — a single-centre prospective cohort of 43 patients

## Częściowe usunięcie przytarczyc *versus* całkowite usunięcie przytarczyc z autoprzeszczepem we wtórnej nadczynności przytarczyc — jednoośrodkowe, prospektywne badanie w grupie 43 pacjentów

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## Abstract

**Introduction:** The need for parathyroidectomy remains high in the group of patients on long-term dialysis with medically refractory secondary hyperparathyroidism (sHPT). We aim to compare the results after subtotal parathyroidectomies (sPtx) and total parathyroidectomies with autotransplant (tPtx + AT) performed for sHPT at a single referral centre.

**Material and methods:** This prospective study comparatively analysed sPtx and tPtx + AT performed in our department between February 2010 and December 2014. We followed-up both surgical techniques, with respect to the main clinical symptoms, laboratory data, mortality, and recurrent disease.

**Results:** Forty-three patients on whom we performed 26 sPtx and 19 tPtx + AT were entered in the study. There were no statistically significant differences between groups as far as demographic and preoperative clinical data are concerned. We did not encounter postoperative mortality in either of the groups. The follow-up period was significantly longer for the sPtx group ($p = 0.04$). The immediate postoperative serum calcium levels were significantly lower in the tPtx + AT group ($p = 0.009$). Definitive hypoparathyroidism was encountered in two patients in the sPtx group (8.3%) and in one from the tPtx + AT group (5.26%). Four patients from the sPtx group (16.6%) and three from the tPtx + AT group (15.78%) died during the follow-up due to causes unrelated to parathyroidectomy. Overall we had two recurrences in the sPtx group and none in the tPtx + AT group ($p = 0.57$).

**Conclusions:** In our opinion both techniques have comparable results concerning the clinical and laboratory outcomes and rates of postoperative hypoparathyroidism, at least in short- and medium-term follow-up. **(Endokrynol Pol 2016; 67 (2): 202–209)**

***Key words:*** *subtotal parathyroidectomy; total parathyroidectomy; autotransplant*

## Streszczenie

**Wstęp:** Potrzeba wykonywania zabiegu usunięcia przytarczyc pozostaje na wysokim poziomie wśród grupy pacjentów poddawanych długoterminowej dializie cierpiących na wtórną nadczynność przytarczyc (sHPT) oporną na leczenie**.** W niniejszym badaniu, autorzy porównują wyniki po częściowym usunięciu przytarczyc (sPtx) oraz całkowitym ich usunięciu z autoprzeszczepem (tPtx + AT) wykonanym dla sHPT w jednym ośrodku referencyjnym.

**Materiał i metody:** Niniejsze prospektywne badanie dokonuje analizy porównawczej sPtx oraz tPtx + AT, wykonanych w miejscu pracy autorów w okresie od lutego 2010 do grudnia 2014 roku. Autorzy porównali obie techniki operacyjne w związku z głównymi objawami klinicznymi, badaniami laboratoryjnymi, śmiertelnością oraz nawrotowością choroby.

**Wyniki:** W badaniu wzięło udział 43 pacjentów: 26 poddano sPtx, a 19 tPtx + AT. Pomiędzy grupami nie było znaczących różnic statystycznych, jeśli chodzi o dane demograficzne i przedoperacyjne dane kliniczne. Nie stwierdzono śmiertelności pooperacyjnej w żadnej z grup. Okres obserwacji trwał zdecydowanie dłużej w grupie sPtx ($p = 0,04$). Stężenie wapnia w osoczu mierzone zaraz po operacji było znacznie niższe w grupie tPtx + AT ($p = 0,009$). Całkowita niedoczynność przytarczyc zidentyfikowano u dwóch pacjentów w grupie sPtx (8,3%) oraz jednego z drugiej grupy (5,26%). Czterech pacjentów z grupy sPtx (16,6%) i trzech z grupy tPtx + AT (15,78%) zmarło podczas okresu obserwacji z powodów niezwiązanych z usunięciem przytarczyc. Ogółem zidentyfikowano dwa nawroty choroby w grupie sPtx i żadnego z drugiej grupie ($p = 0,57$).

**Wnioski:** W opinii autorów, obie techniki dają porównywalne wyniki, biorąc pod uwagę wyniki laboratoryjne oraz kliniczne, a także wskaźniki pooperacyjnej niedoczynności przytarczyc, przynajmniej w krótko- i średnioterminowym okresie obserwacji.
**(Endokrynol Pol 2016; 67 (2): 202–209)**

***Słowa kluczowe:*** *częściowe usunięcie przytarczyc; całkowite usunięcie przytarczyc; autoprzeszczep*

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## Introduction

Secondary hyperparathyroidism (sHPT), frequently encountered among patients with end-stage renal disease (ESRD) on haemodialysis, is a potentially severe complication that can lead to metabolic bone disease and severe cardiovascular events [1]. In spite of improved conventional medical therapy, the need for parathyroidectomy remains high, especially in the group of patients on long-term dialysis with medically refractory sHPT [2, 3]. Among surgical indications in sHPT few are generally accepted, i.e. worsening clinical symptoms under correct medical therapy, high values of serum intact parathyroid hormone (iPth) and phosphorus, calciphylaxis, and osteitis fibrosa cystica [4, 5].

The optimal surgical procedure in sHPT treatment is far from established, this issue being under continuous controversy in literature. The remnant-conserving techniques of parathyroidectomy consist of either subtotal parathyroidectomy (sPtx) —removing all parathyroid tissue but a small portion of a normal appearing gland which is left in the neck or total parathyroidectomy with autotransplant (tPtx + AT) — removing all parathyroid tissue and reimplanting at a distance small pieces of tissue in well-vascularised muscular structures. Even if both techniques are now under intense criticism, mainly due to their high recurrence rates of sHPT, they remain the most recommended and widely performed surgical procedures [1, 3]. Recently another technique, total parathyroidectomy without autotransplant (tPtx), re-emerged as a trustworthy surgical solution in severe sHPT, especially in patients with low perspective for renal transplantation [1, 3, 6].

The present study comparatively analyses a series of patients who underwent sPtx or tPtx + AT at a single referral centre. Our aim was to evaluate and compare the short-, medium-, and long-term follow-up results after both surgical techniques, with respect to the main clinical symptoms, laboratory data, mortality, and recurrent disease and to define a surgical strategy in our daily practice.

## Material and methods

This is a prospective study of a cohort of patients with ESRD on haemodialysis, submitted to parathyroidectomy for severe sHPT between February 2010 and December 2014 at the Second Department of General Surgery, the University of Medicine and Pharmacy Tîrgu Mures. During this period we performed three types of surgeries: sPtx, tPtx + AT, and total parathyroidectomy without autotransplantation (tPtx). All surgeries were done by the same surgical team and the initial experience was previously reported [7, 8]. We included patients with severe, medically refractory sHPT, who underwent either sPtx or tPtx + AT during the aforementioned period and were followed-up at least three months after the surgery. Our inclusion criteria for parathyroidectomy were: very high levels of intact parathyroid hormone (iPth > 800 pg/mL) unresponsive to available medical therapy; severe clinical symptoms such as osteoarticular pains, pruritus, and muscle weakness; radiological findings indicating severe osteoporosis, bone changes, or osteitis fibrosa cystica; and high levels of serum calcium and phosphorus (serum calcium-phosphate production over 70 mg/dL). We excluded from the present study patients submitted to total parathyroidectomy without autotransplantation and those with a follow-up period under three months, no matter the type of surgery.

The diagnosis was established on laboratory and imagistic data. Preoperative localisation studies included neck ultrasonography and Tc-99m sestamibi parathyroid scans, the latter being inconstantly used. All patients were loaded with vitamin D and were dialysed the day before the operation, the next dialysis being done on the first postoperative day. All patients were informed about the aim of this study and provided written informed consent, and the study was done with the consent of the Hospital Ethics Committee.

### *Surgical procedures*

The treatment options for the studied cohort were sPtx and tPtx + AT, both surgeries being performed under general anaesthesia. As a general principle we constantly dissect the recurrent laryngeal nerves at the beginning of both procedures. We did not routinely perform thymectomy if four parathyroid glands were confidently identified. Subtotal parathyroidectomies were performed by leaving one third to one fourth of a cvasinormal well-vascularised inferior gland with its neopedicle (small mediastinal or thymic vessels) in a suprasternal position. Total parathyroidectomies with autotransplant were performed by implanting 9–15 small pieces (1 $mm^3$) of non-nodular parathyroid tissues in 3–4 muscular pockets of sternocleidomastoid muscle, marked with a metallic clip. In a few cases we encountered associated thyroid pathology requiring lobectomies or total thyroidectomies. All parathyroid glands were weighed, measured, and sent for pathological testing.

### *Postoperative management and follow-up*

All patients who underwent both procedures were carefully evaluated before parathyroidectomy in terms of clinical data, laboratory parameters, and results of localisation studies. The first postoperative dialysis was performed on postoperative day 1. In the first

**Table I.** *Demographic and clinical data of the studied patients*
**Tabela I.** *Dane demograficzne i kliniczne pacjentów ujętych w badaniu*

| | sPtx (n = 24) | tPtx + AI (n = 19) | p value |
|---|---|---|---|
| Sex (males/females), no (%)# | 8 (33.3)/16 (66.7) | 9 (47.4)/10 (52.6) | 0.53 |
| Age (years), mean ± SD* | 50.0 ± 10.6 | 51.1 ± 11.1 | 0.72 |
| Dialytic age (years), mean ± SD* | 8.35 ± 2.5 | 9.14 ± 2.7 | 0.32 |
| Preoperative iPth [pg/mL] Median (min–max)** | 2131 (1141–10000) | 2439 (840–6115) | 0.88 |
| Preoperative total serum calcium [mg/dL], mean ± SD* | 9.02 ± 0.84 | 9.50 ± 0.51 | 0.17 |
| Preoperative serum phosphorus [mg/dL], mean ± SD* | 5.86 ± 1.31 | 6.17 ± 0.76 | 0.35 |
| Preoperative AlkPhos [U/L], Median (min–max)** | 575.0 (196.1–2636) | 587.0 (84–987.0) | 0.80 |
| Associated thyroid pathology, n (%)# | 4 (16.6) | 3 (15.8) | 0.73 |
| In hospital stay(days) Median (min–max)** | 4 (2–9) | 3 (2–6) | 0.24 |
| Persistent hyperparathyroidism | 2 (8.3) | 0 (0.0) | 0.57 |
| Follow–up (months) Median (min–max)** | 38 (6–52) | 18 (1–36) | 0.03 |
| Recurrent sHPT, n (%)# | 2 (8.3) | 0 (0.0) | 0.57 |
| Deaths during follow–up, n (%)# | 4 (16.6) | 3 (15.7) | 0.73 |

#chi square test; *data expressed as mean ± SD, Student test; **data expressed as median (min–max), Mann Whitney test

postoperative weeks we carefully monitored calcium levels and, when considered appropriate, calcium gluconate infusion with oral alphacalcidol was administered. In the follow-up period we evaluated patients at three-month intervals as regards improvement of symptoms, iPth, total calcium, phosphate, and alkaline phosphatase (AlkPhos) serum levels. We considered as a short follow-up the first six postoperative months, and as a medium follow-up the next 6-18 months; after this time frame we defined the long-term follow-up period. Three patients from our group were lost to follow-up. Hypoparathyroidism was considered when iPth levels remained constantly low (under 12 pg/mL) one year after parathyroidectomy, with normal or low serum calcium levels under appropriate supplementation. We defined persistent or recurrent HPT according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (K-DOQI) [9].

### *Statistical analysis*

All statistical calculations were performed using Graph Pad Software, San Diego, California, USA. We tested the normal distribution for continuous variable using Kolmogorov-Smirnov test. We characterised them as mean and standard deviation of the mean (SD) for variables with normal distribution, or as median and 25–75 percentiles for variables with abnormal distribution. We chose adequate statistical tests according to data distribution. The frequencies of nominal variables were compared with the chi-square test. Differences between mean age values were determined by Student *t*-test. Differences in values between compared postoperative variables were determined by Kruskal-Wallis test (associated with the Dunns multiple comparison test) and ANOVA test (associated with the Bonferroni multiple comparison test). All the tests were interpreted relative to the significance threshold p = 0.05, and statistical significance was considered for p-values below the significance threshold value.

## Results

Forty-three patients on whom we performed 45 parathyroidectomies were entered in the study. The general cohort was divided into two groups: a sPtx group, including 24 patients (55.81%) with a mean age ± SD of 50.0 ± 10.6 years, on whom we performed 26 parathyroid surgeries and a tPtx + AT group of 19 patients (44.18%) with a mean age ± SD of 51.1 ± 11.1 years. There were no statistically significant differences between groups as far as demographic, causes of ESRD and preoperative clinical data are concerned (Table I).

Patients presented with various clinical symptoms, but the main complaints were arthralgia, myalgia and bone pains, muscle weakness, and pruritus. We had one female patient in the sPtx group, who presented

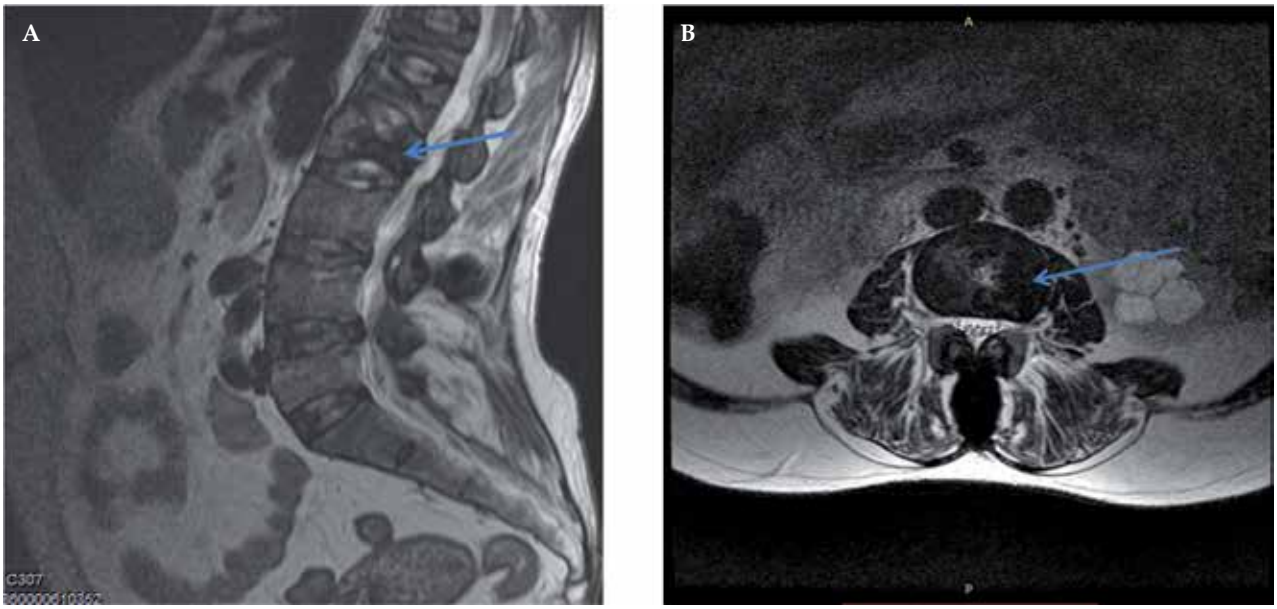




**Figure 1A.** *Sagittal T2 weighted sequence of the thoracic and lumbar spine shows at the level of the body of Th 10th an expansile lesion with heterogenous signal.* **B.** *Axial T2-weighted image at the level of Th 10th, brown tumour of the body of Th 10th vertebrae*

**Rycina 1A.** *Obraz T2-zależny kręgosłupa w odcinku piersiowym i lędźwiowym w projekcji strzałkowej pokazuje na poziomie dziesiątego kręgu piersiowego rozległą zmianę o heterogenicznym sygnale.* ***B.*** *Obraz T2-zależny w projekcji osiowej pokazuje guz barwy brązowej na poziomie dziesiątego kręgu piersiowego*

multiple osseous lesions consistent with brown tumours, including an extremely rare multilevel spine localisation (Fig. 1A, B). She had a massively raised preoperative serum iPth level (10 000 pg/mL) showing a severe secondary hyperparathyroid status, unresponsive to medical treatment. We also noted calcification or deposits of calcium in soft tissues in some patients.

Patients from both groups had markedly elevated preoperative serum iPth, with median values above 2000 pg/mL. We also frequently noted hypophosphataemia and high levels of AlkPhos, without significant differences between groups; not all of our patients had elevated preoperative calcium levels.

Regarding preoperative imaging studies, both cervical ultrasonography and 99mTc sestamibi failed to identify all enlarged parathyroids. In the last period we performed only cervical ultrasonography as a routine preoperative localisation study, 99mTc sestamibi being considered only for reinterventions.

Associated thyroid pathology was encountered in seven patients from both groups. Two total thyroidectomies (TT) and two lobectomies where performed in the sPtx group, while two TT and one lobectomy were done in the second group. We had one patient in the sPtx group with a TT for a multinodular goitre in whom the final histopathological report revealed a papillary microcarcinoma. In the other group we encountered a patient with a papillary thyroid carcinoma; here we performed TT and an ipsilateral central compartment lymphadenectomy.

We did not encounter postoperative mortality in either group; in the sPtx group we noted two patients with temporally dysphonia after operation and one cervical haematoma after the first postoperative dialysis, requiring surgical evacuation. In the immediate postoperative period (30 days) seven patients (29.16%) from this group presented minor episodes of hypocalcaemia ("hungry bones" syndrome), rapidly restored after calcium infusions. In the same group we also had two cases of persistent hyperparathyroidism (immediate iPth values > 300 pg/mL), both with only three parathyroids initially resected. One patient was reoperated on after two months when we found a fourth (missed) inferior parathyroid in the anterior mediastinum. The second patient also had a repeated neck exploration; here a left superior gland was found in an upper retroesophageal ectopy. This latter patient subsequently developed a postoperative hypoparathyroidism, with iPth values constantly below 10 pg/mL, but with a moderate hypocalcaemia and no related clinical symptoms. In the tPtx + AT group we did not encounter persistent hyperparathyroidism cases; here we had one case of temporary dysphonia and nine patients (47.36%) with postoperative hypocalcaemia. The average length of in-hospital stay was four days (range 2–9 days) in the sPTx group and three days (range 2–6 days) in the tPtx + AT group.

**Table II.** *Sequential values for of iPth, serum calcium, phosphorus and AlkPhos during follow-up for both groups; values are calculated for short (under 6 months), medium (6–18 months), and long-term follow-up (over 18 months)*

**Tabela II.** *Wartości sekwencyjne dla iPth, wapnia w osoczu, fosforu i fosfatazy alkalicznej w okresie obserwacji dla obu grup; wartości liczone są dla krótkiego (poniżej 6 miesięcy), średniego (6–18 miesięcy) oraz długiego okresu obserwacji (powyżej 18 miesięcy)*

| Variables | sPtx (n = 24) | tPtx + Al (n = 19) | P value |
|---|---|---|---|
| Ca (1 month) [mg/dL] mean ± SD* | 8.47 ± 1.16 | 7.56 ± 0.96 | 0.009 |
| Ca (short) [mg/dL] mean ± SD* | 8.21 ± 1.21 | 7.84 ± 0.55 | 0.22 |
| Ca (medium) [mg/dL] mean ± SD* | 8.62 ± 0.91 | 8.26 ± 0.61 | 0.21 |
| Ca (long) [mg/dL] mean ± SD* | 8.68 ± 0.80 | 8.66 ± 0.74 | 0.96 |
| P (1 month) [mg/dL] mean ± SD* | 3.91 ± 1.61 | 3.25 ± 0.61 | 0.10 |
| P (short) [mg/dL] mean ± SD* | 4.37 ± 1.34 | 3.68 ± 0.78 | 0.05 |
| P (medium) [mg/dL] mean ± SD* | 5.32 ± 1.21 | 4.11 ± 1.21 | 0.01 |
| P (long) [mg/dL] mean ± SD* | 5.38 ± 1.17 | 4.86 ± 1.14 | 0.32 |
| iPTH (1 month) [pg/mL] median (min–max)** | 28 (3–1263) | 20 (9–68) | 0.77 |
| iPTH (short) [pg/mL] median (min–max)** | 23.7 (0.8–86.7) | 36.6 (14–78.15) | 0.10 |
| iPTH (medium) [pg/mL] median (min–max)** | 19.5 (3–199.3) | 38.1 (14.3–107.8) | 0.03 |
| iPTH (long) [pg/mL] median (min–max)** | 45.3 (3–724.6) | 61.2 (4.2–100.7) | 0.85 |
| AlkPhos (1 month) [U/l] median (min–max)** | 452 (123–2236) | 365 (78–767) | 0.20 |
| AlkPhos (short) [U/l] median (min–max)** | 204.6 (39.6–416.5) | 170.5 (61–321.0) | 0.29 |
| AlkPhos (medium) [U/l] median (min–max)** | 123.9 (68.5–390.7) | 103.0 (81.5–165.0) | 0.65 |
| AlkPhos (long) [U/l] median (min–max)** | 113.9 (58.5–291.2) | 97 (81.5–315.0) | 0.71 |

*Data expressed as mean ± SD Student test; **Data expressed as median (min–max), Mann Whitney test; short — follow-up under 6 months; medium — follow-up 6-18 months; long — follow-up above 18 months

The median follow-up period was significantly longer for the sPtx group than for the tPtx + AT group (38 months *vs.* 18 months, respectively); three patients from the sPtx group were lost to follow-up. All the rest were carefully evaluated at three-month intervals in terms of clinical symptoms and biochemical parameters. Sequential values of iPth, serum calcium, phosphorus, and AlkPhos during follow-up for both groups are presented in Table II.

The serum iPth levels decreased significantly in both groups when compared with preoperative values, but without postoperative differences between them. The severe hyperparathyroidism was corrected in 100% of patients in the tPtx + AT group and in 91.6% in the other group. The only significant difference between groups was in immediate (one-month) postoperative serum calcium levels, which were significantly lower in the tPtx + AT group, with a mean ± SD value of 7.56 ± 0.96 in this group and 8.47 ± 1.16 in the sPtx group ($p = 0.009$). Indeed, in the tPtx + AT group we had four patients who had serum calcium below 7 mg/dL in the first postoperative month and symptoms related

**Table III.** *Type of parathyroid hyperplasia in the resected parathyroids from both groups*
**Tabela III.** *Typ rozrostu przytarczyc w wyciętych przytarczycach w obu grupach*

| Type of parathyroid hyperplasia | sPtx group (24 cases) | tPtx + AT group (19 cases) | P value |
|---|---|---|---|
| Nodular, n (%)# | 14 (58.33) | 11(57.89) | 0.77 |
| Diffuse, n (%)# | 7 (29.16) | 5 (26.31) | 0.89 |
| Mixed, n (%)# | 3 (12.50) | 3 (15.78) | 0.87 |

#chi square test



to hypocalcaemia, requiring important supplementation with calcium infusions and vitamin D analogues. During follow-up the serum calcium levels were comparable between the analysed groups, being found in the normal range. Definitive hypoparathyroidism was encountered in two patients in the sPtx group (8.3%) and one from the other group (5.26%), all these patients having iPth values below 10 pg/mL after one year from parathyroidectomy, under proper treatment. Four patients from the sPtx group (16.6%) and three from the other group (15.78%) died during the follow-up due to causes unrelated to parathyroidectomy. One patient from the sPtx group, who died 28 months after the surgery, was diagnosed with sHPT recurrence, having an iPth level above 500 pg/mL, well tolerated under medication. Overall we had two recurrences in the sPtx group and none in the other group, but the differences were not statistically significant. Definitive histological examinations of the resected parathyroids showed different patterns of nodular hyperplasia, diffuse hyperplasia, or mixed aspects in both groups, without significant differences (Table III).

## Discussion

The need for parathyroidectomy increases with the time on dialysis and survival of patients with stage 5 chronic renal disease [2, 4]. In Eastern European countries the prevalence of renal replacement therapies and renal transplant incidence are still very low when compared to Western counterparts [8, 10]. Even if in Romania we frequently note patients on long-term haemodialysis, as far as we know the number of parathyroidectomies performed per annum is lower than anticipated [8]. Calcimimetics and other new therapeutic agents, i.e. phosphate binders and vitamin D analogues, have demonstrated efficacy in sHPT. The treatment with cinacalcet is expensive but is supported in our country through a National Health System program, thus an important number of patients benefited from it throughout their dialytic periodic; the lack of response or contraindications to the treatment are among indications for parathyroidectomy.

Three types of surgeries have been proposed in sHPT, two of them (i.e sPtx and tPtx + AT together with their variations) being grouped as remnant-conserving techniques [1]. The philosophy behind those techniques resides in the preservation of a normal or less modified (non-nodular) portion of a gland, which is abandoned in the neck or autotransplanted in well-vascularised muscular regions [11, 12]. The third technique, total parathyroidectomy without autotransplantation (tPtx), was initially severely criticised mainly for the long-term hypoparathyroidism induced and its consequences on bone metabolism [13]. Recent papers, however, have revived tPtx as a trustworthy technique with comparable results in short- and medium-term follow-up [6, 14, 15].

The present study comparatively analysed two groups of patients submitted to sPtx or tPtx + AT in our surgical department. Both groups were similar as regards demographics, time on dialysis, or causes of ESRD. Our patients underwent parathyroidectomy because of refractory medical sHPT, a state in which excessive parathyroid hormone secretion no longer responds to conventional medical treatment, here including adequate dialysis [7].

The indications for parathyroidectomy are still debated in the literature, but similarly to others [1, 4, 5] we consider generally accepted high iPth levels (above 800 pg/mL), disabling clinical picture with osteoarticular pains and bone changes, pruritus, muscular weakness, along with hyperphosphataemia, and less commonly hypercalcaemia. This clinical and laboratory picture was constantly seen in both our groups. Undeniably we frequently noted increased even huge values of preoperative serum iPth, hyperphosphataemia and increased values of AlkPhos in response to intense bone metabolism. Thus, we had patients with severe bone changes, pathological fractures, and other aspects that characterised osteitis fibrosa cystica. As previously mentioned, this clinical picture corroborated with the constant discovery of "macroscopically" nodular glands during surgeries betraying the long evolution of the disease, its "tertialisation", and even surgery delays [7, 8].

The role of localisation studies in sHPT diagnosis is also debatable. Even if scintigraphy (99mTc-MIBI) is

considered the best and most sensitive test [1, 3, 16], its role in locating all parathyroid glands before surgery is doubtful, being less important when compared with the surgeon's experience [16]. Scintigraphy becomes important in redo procedures for relapsing or persistent hyperparathyroidism, especially when associated with high-resolution cervical ultrasonography [1, 16]. We frequently used both imagistic techniques at the beginning of our experience (first 15–20 cases), but in spite of this we encountered two cases of persistent hyperparathyroidism in that period (missed glands), a fact which we interpret now as reflecting an inherent learning curve.

Subtotal parathyroidectomy was the first surgical technique described in the treatment of sHPT [11]. As we mentioned above, we preferred a "modified" sPtx in which we placed the chosen inferior parathyroid gland in a subcutaneous position preserving a vascular "neo-pedicle" (small mediastinal and thymic vessels). We then resected the gland subtotally, preserving a remnant that has in principle the dimension of a normal parathyroid [7]. Regarding tPtx + AT we used the sternocleidomastoid muscle as receptor for autotransplantation in all cases. Even if this technique is criticised by some authors [1, 3], claiming the difficulties in localisation of the neck transplant in cases of recurrent graft HPT, we favoured it due to its simplicity and rapidity. Nonetheless, we constantly mark the autotransplant regions with metallic clips, thereby facilitating a possible reintervention. Cervical thymectomy is favoured by some authors [3, 17] but is still far from being considered a standard of care in sHPT. As far as we know there is an ongoing randomised controlled trial (TOPAR PILOT-Trial), started in 2007, which aims to evaluate tPtx with or without thymectomy [9]. We did not routinely perform cervical thymectomy in our groups if four glands were confidently identified, an opinion also supported by others [18]. Furthermore, there are authors who consider the opportunity of a central compartment lymphadenectomy (CCL) in sHPT bearing in mind the frequency of supranumerary parathyroids in sHPT [3]. We did not consider central CCL as a routine procedure in either group. However, we performed an ipsilateral CCL in a patient with associated papillary thyroid carcinoma. We did not have the opportunity to use intraoperative parathyroid hormone (IOPTH) assessment in monitoring the surgery results, a procedure otherwise less straightforward for sHPT than for primary hyperparathyroidism. Instead we constantly determined immediate postoperative iPth values in the first week after the surgery.

Generally, remnant-conserving techniques are associated with good clinical outcome and functional improvement [6, 19–21]. Regardless of the surgical procedure we noted a rapid improvement of clinical symptoms after both types of parathyroidectomies, mainly those that concerned bone pains, pruritus, and muscle weakness. After surgery iPth levels dropped significantly in both groups, without statistical differences. The only significant difference was related to the postoperative serum total calcium levels which, as expected, were lower in the tPtx + AT group. As a consequence, we encountered more patients with "hungry bone" syndrome in this latter group, requiring higher doses and prolonged administration of calcium infusions and alphacalcidol.

We did not encounter in-hospital mortality in either series; the postoperative surgery-related complications were minor and transitory in both groups. We did have two patients with persistent HPT in the sPTx group, both being reoperated on, initially with good postoperative outcome. One of these patients presented iPth values below 10 pg/mL a few months after reintervention, values which remained constantly low during follow-up, but without clinical symptoms. Hypoparathyroidism could be determined in this case by the "low quality" of the autotransplanted parathyroid tissue, harvested from a left superior parathyroid in a retroesophageal ectopy and with important morphological changes. None of the patients in the tPtx + AT group had persistent HPT, a fact which may be interpreted as being related to the learning curve, those patients being operated later on in the time line of this study.

At the end of the study 30 patients (69.76%) were free from disease, three patients had sHPT recurrence, and three patients from the sPtx group were lost to follow-up. Furthermore, seven patients (32.3%) from both groups died during follow-up, from different causes unrelated to parathyroidectomy. Undoubtedly the latter percentage is rather high when compared with other studies [22, 23], but it reflects the clinical reality in our region: patients on long-term dialysis, with advanced disease, and with low perspective of renal transplantation. Of interest, none of our patients was submitted to renal transplant during the analysed period.

Remnant-conserving techniques are generally related to higher relapse rate, between 5–80% [1]; Rothmund et al. randomised 40 patients with sHPT to either sPtx or tPtx + AT, describing significantly less recurrences after the latter surgical technique [24]. In spite of this clear statistical conclusion, the study was to small to determine a standardisation of surgical approach in sHPT; furthermore, other retrospective studies, including a meta-analysis of 53 publications regarding surgical treatment of sHPT, did not show significant differences between the two aforementioned techniques [3, 19]. Our recurrence rates were comparable in either group and rather low when compared with the above-mentioned

numbers; however, at least for the tPtx + AT group, the follow-up period was only 18 months, thus a clear conclusion is difficult to be drawn. It seems that tPtx has reappeared as a "rehabilitated" surgical technique, after a long period of controversial discussion [6, 14, 16, 25, 26]. In the studied period we performed tPtx in few cases, generally in patients with severe and long lasting disease and without a realistic perspective of renal transplantation. Due to the low number of those patients they were excluded from the present analysis.

## Conclusions

Despite improvements in medical therapies, parathyroidectomy remains a solution in a subset of patients with severe refractory sHPT. Over the last decades, there has been considerable controversy as to which of the described parathyroidectomy approaches provide better short- and long-term outcomes, most of the conclusions being contradictory. In spite of its limitations — it is non-randomised, with small sample size per arm and several group selection biases — we believe that our study reflects the reality regarding the clinico-therapeutic particularities of sHPT in our geographical area: patients on long-term dialysis, with advanced disease and with low perspective of renal transplantation. In our opinion both techniques, i.e. sPtx and tPtx + AT, have comparable results concerning the clinical and laboratory outcome and rates of postoperative hypoparathyroidism, at least in short- and medium-term follow-up. As regards the recurrent disease, even if we did not find significant differences between the analysed approaches, it appears that tPtx + AT has a "small advantage" in this issue. Further randomised control trials and meta-analyses are needed to confirm these results.

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